



vehicle

cmpd 15

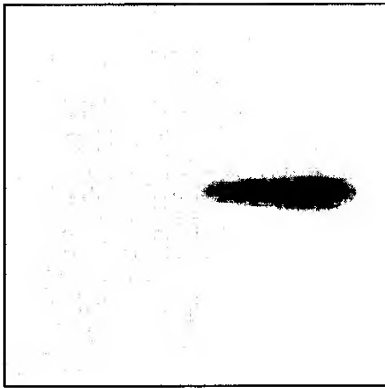


FIG. A -- Compound 15 increases MCIP1 protein expression. Western blot with anti-MCIP1 antibody. Protein prepared from neonatal rat ventricular myocytes exposed to vehicle (DMSO) or compound 15 (10 μ M) for 48 hours.

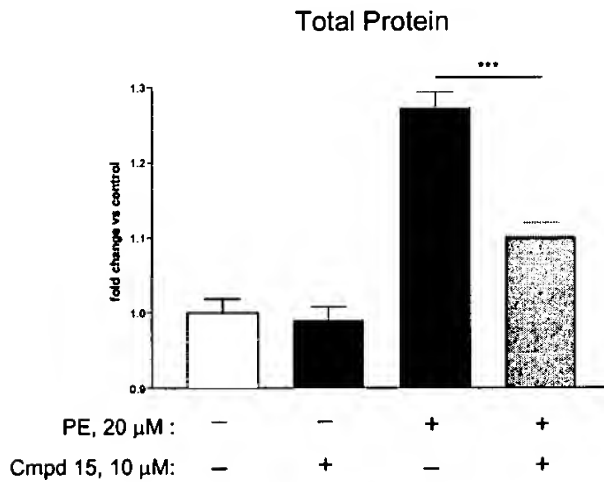


FIG. B -- Compound 15 attenuates phenylephrine-induced increases in total protein. Total protein was measured in neonatal ventricular myocytes exposed to the hypertrophic agonist phenylephrine and compound 15 for a period of 48 hours.

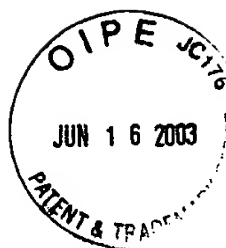
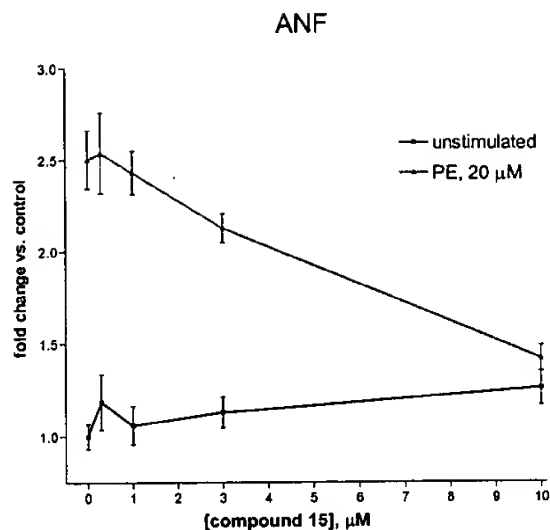


FIG. C -- Compound 15 attenuates phenylephrine-induced increases in secreted ANF. Secreted ANF was measured in neonatal ventricular myocytes exposed to the hypertrophic agonist phenylephrine and compound 15 for a period of 48 hours

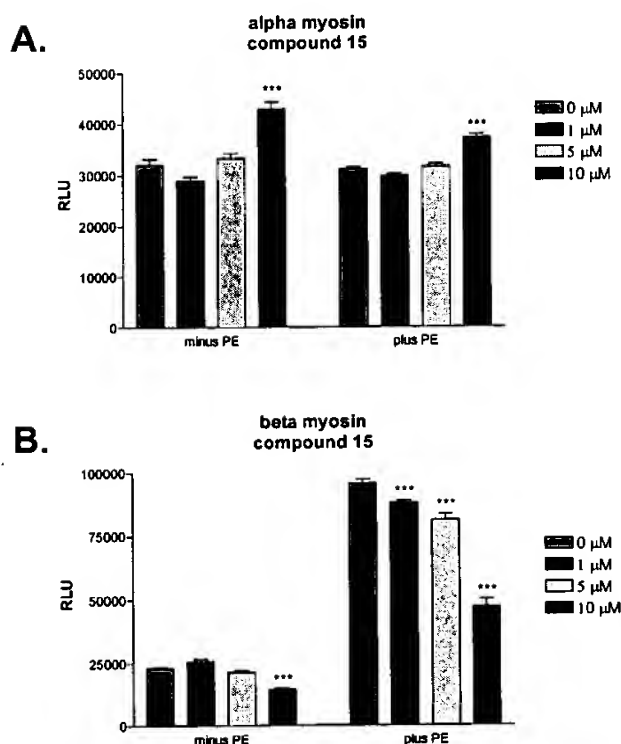


FIG. D -- Compound 15 reverses hypertrophic changes in myosin heavy chain isoform expression in cardiac myocytes. A) Alpha myosin heavy chain expression in neonatal rat ventricular myocytes in the presence or absence of phenylephrine and treated with three concentrations of compound 15. B) Beta myosin heavy chain expression.

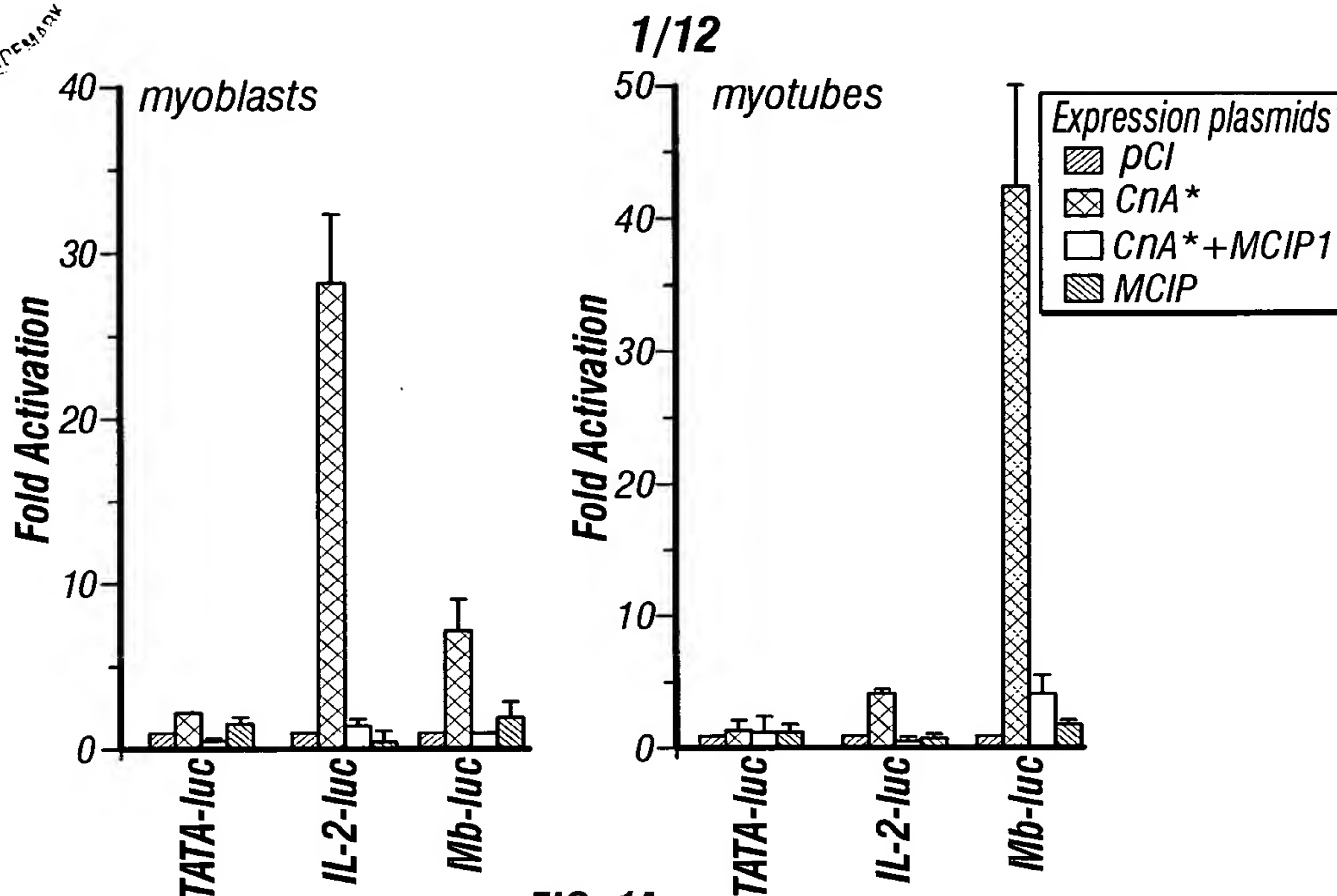


FIG. 1A

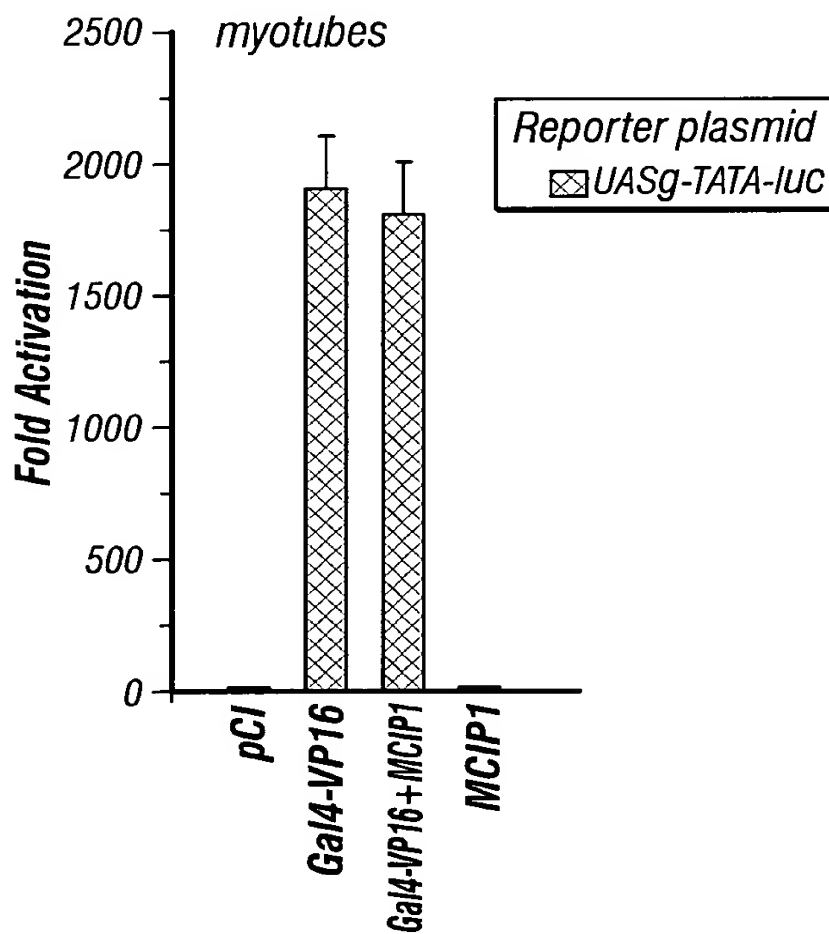


FIG. 1B



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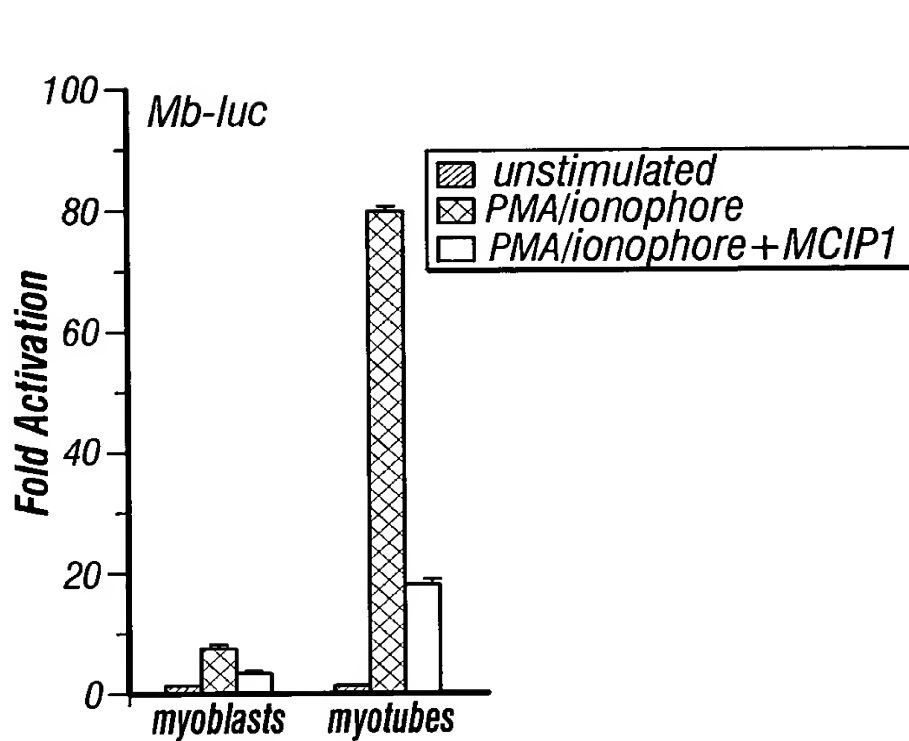


FIG. 2A

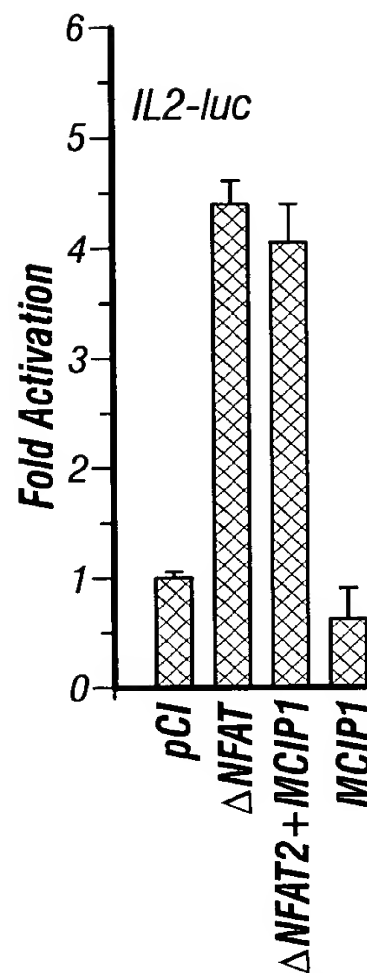


FIG. 2B

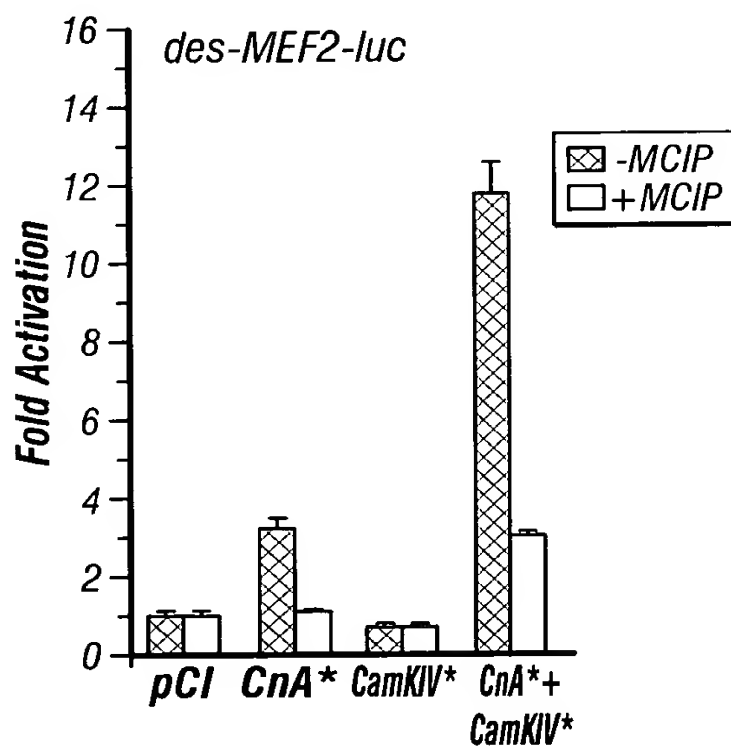


FIG. 2C

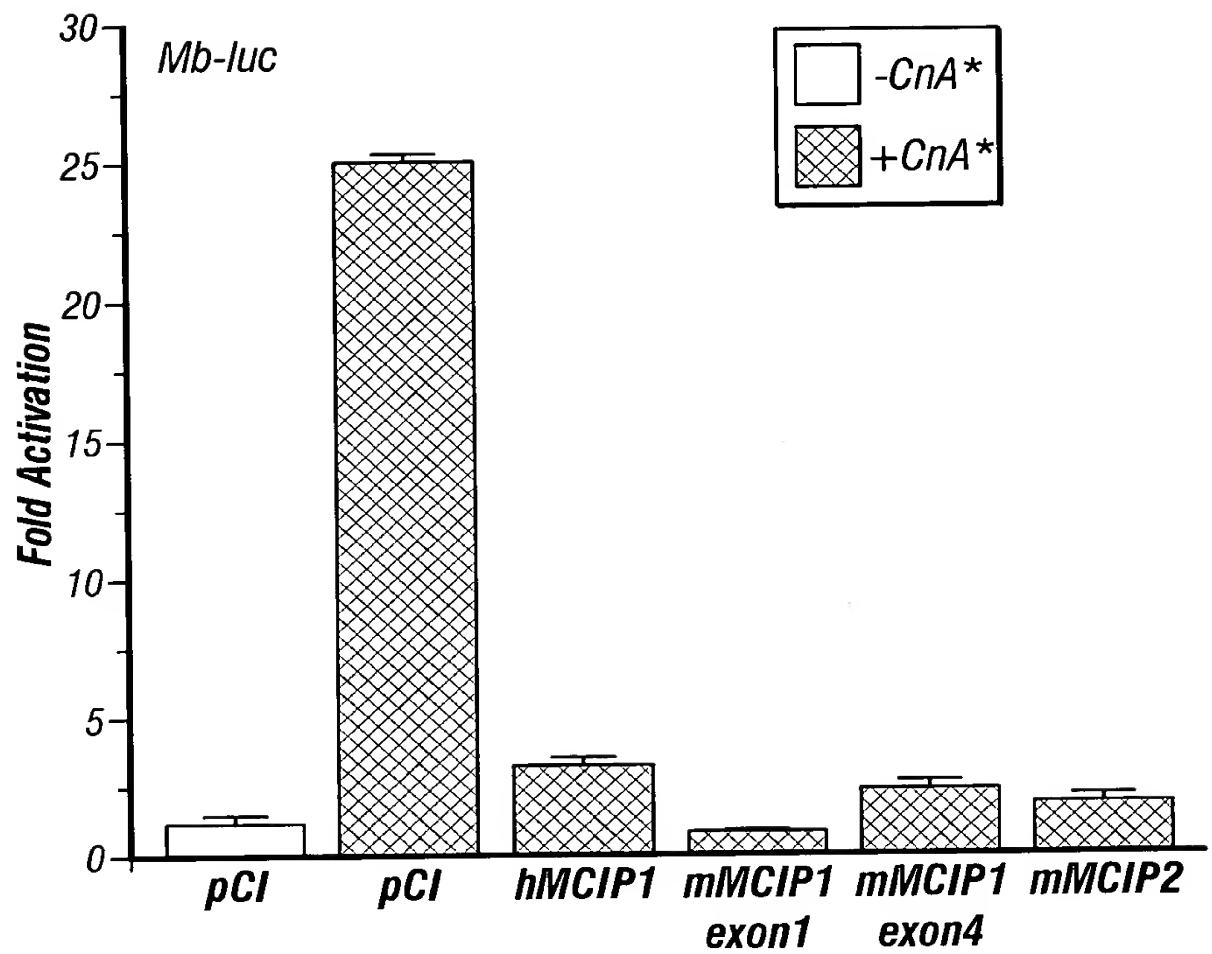


FIG. 3



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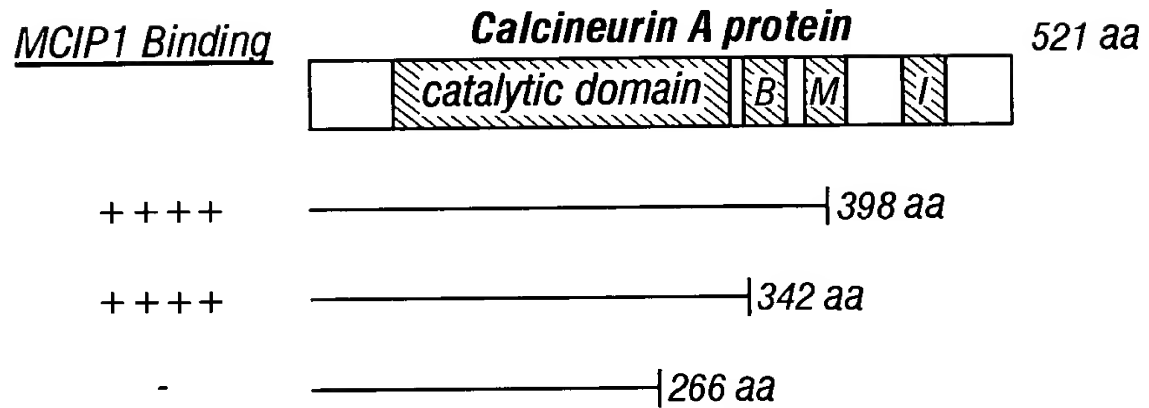


FIG. 4A

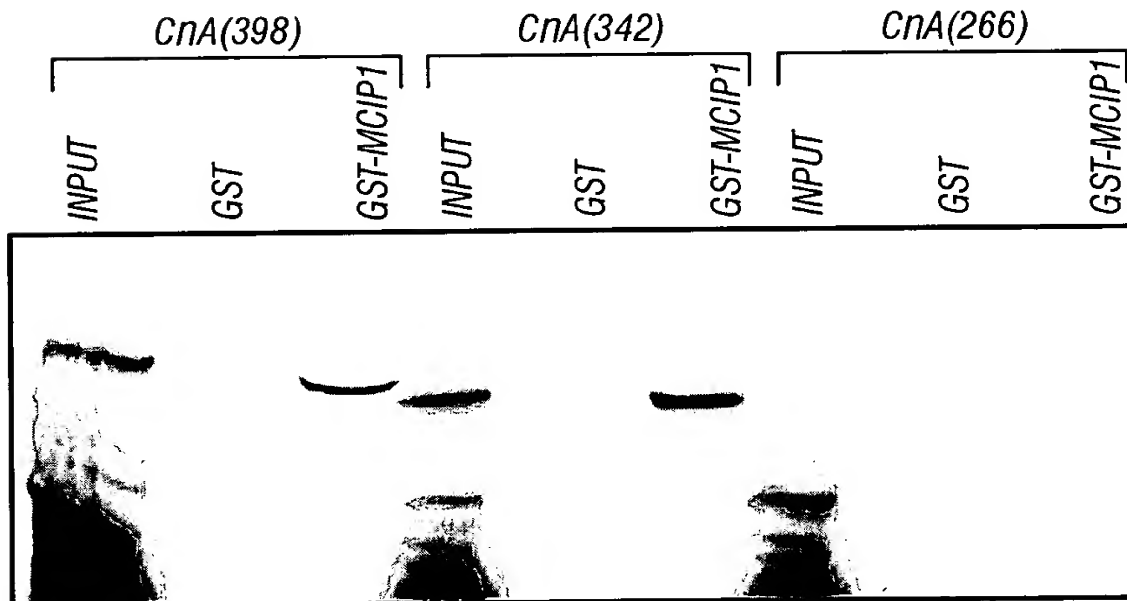


FIG. 4B



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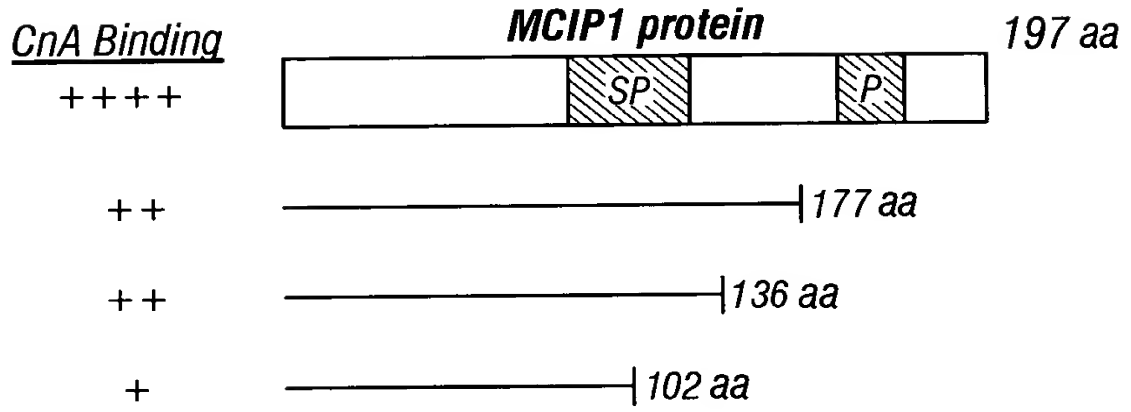


FIG. 5A

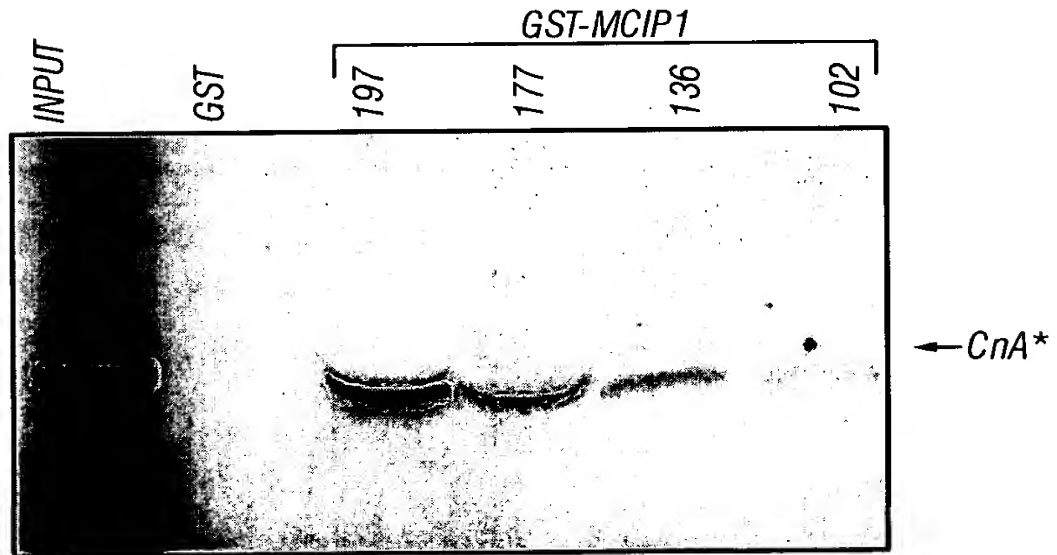


FIG. 5B

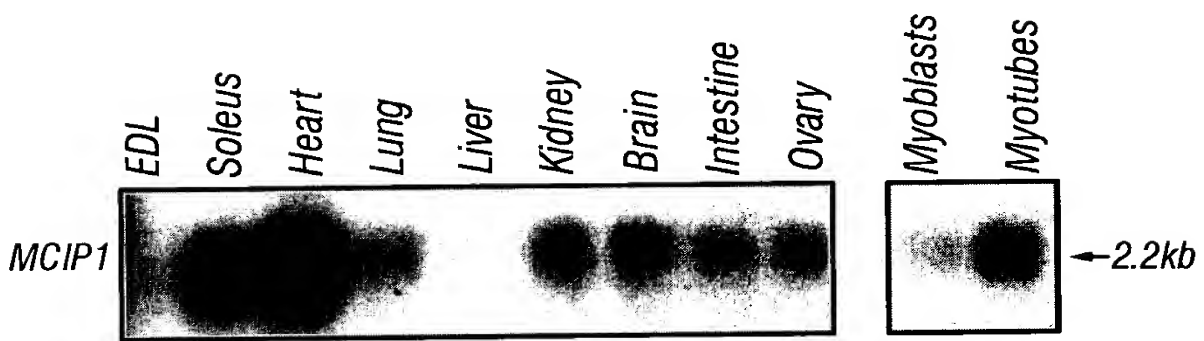


FIG. 6A

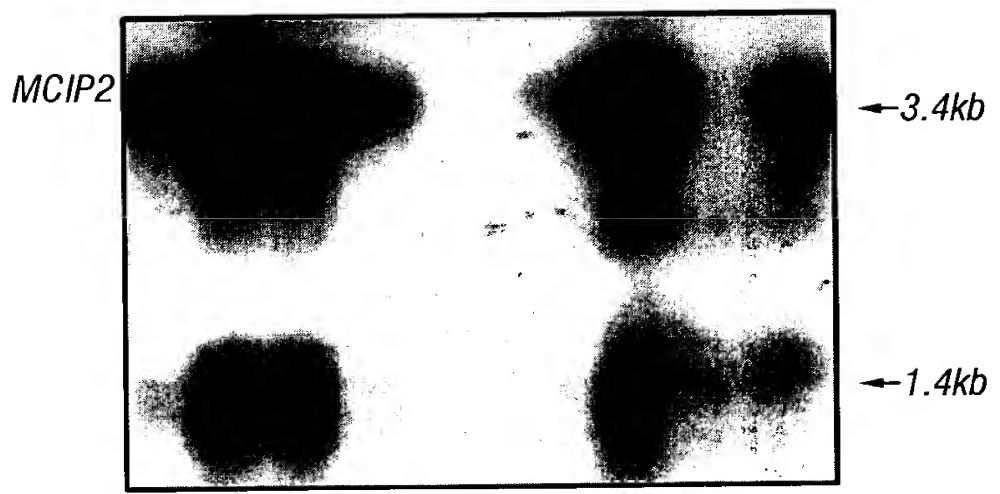


FIG. 6B



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Rank	Fold	Gene	Genbank ID
<i>hypertrophic α-MHC-CnA* vs. wild-type</i>			
1	8.1	Calcineurin-A	AA245461
2	4.0	ANF precursor type B	AA030805
3	3.3	ANF precursor type A	W14325
4	3.1	sk mus LIM protein (FHL1)	AA047966
5	3.0	OSF-2	W81878
→ 6	2.7	MCIP-1	AA200984
7	2.7	EST (mouse)	AA110791
8	2.3	MCPSF (Mouse cleavage and polyadenylation factor)	AA221269
<i>failing α-MHC-CnA* vs. hypertrophic α-MHC-CnA*</i>			
1	3.3	Procollagen XV	W83331
2	2.9	OSF-2	W81878
3	2.8	EST (mouse)	AA124355
4	2.7	Alpha-crystallin	AA231358
→ 5	2.5	MCIP-1	AA200984
6	2.2	Procollagen III	W89883
7	2.1	p53BP2	AA467287
8	2.1	Calcineurin-A	AA245461

FIG. 7



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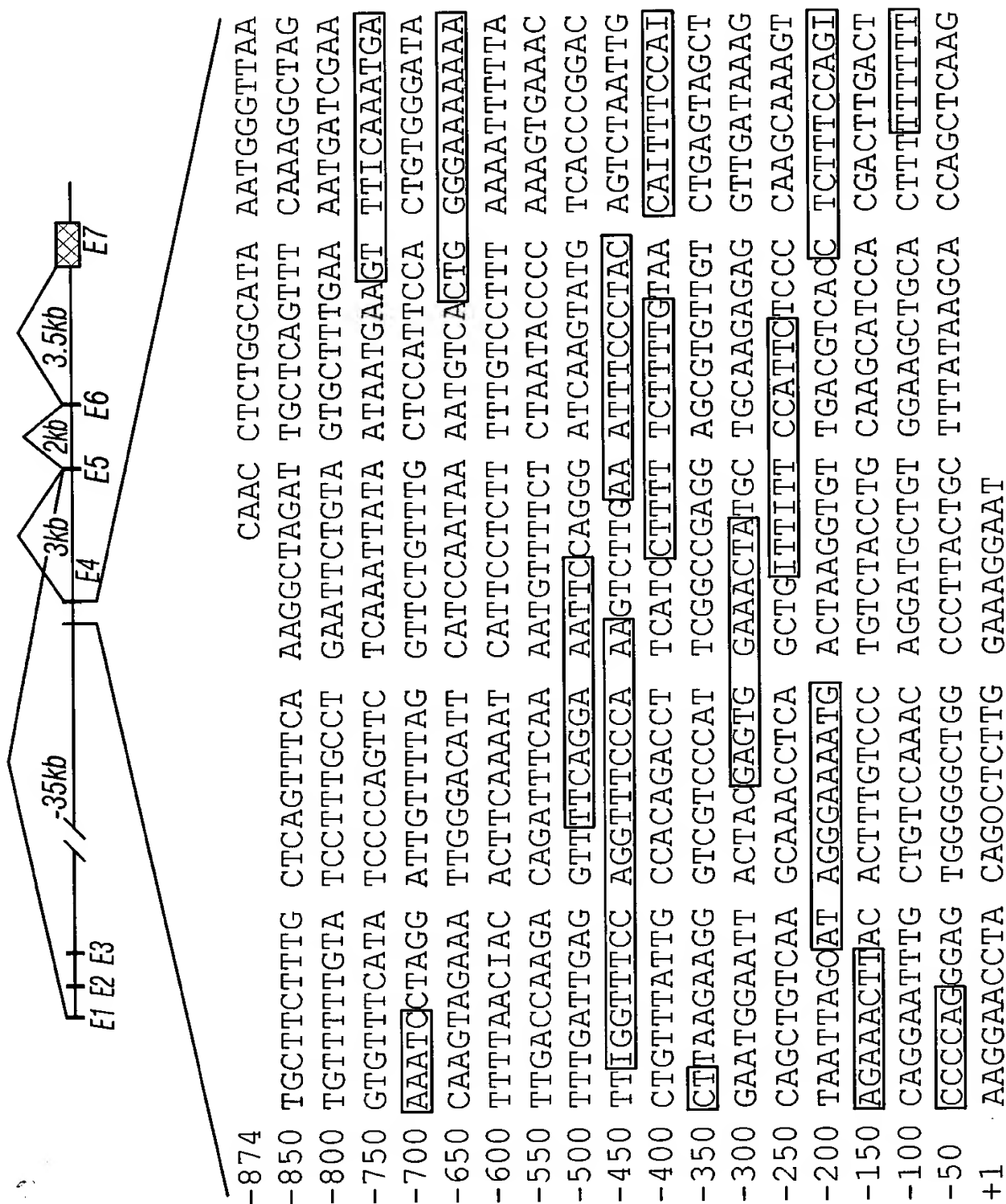


FIG. 8A



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MCIP exon 4 promoter constructs

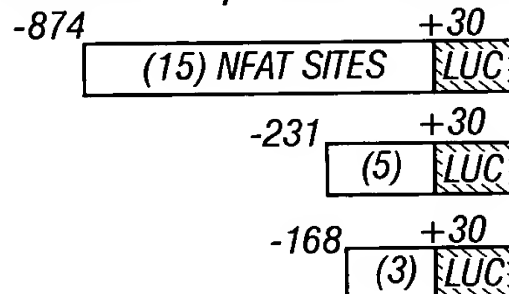


FIG. 8B

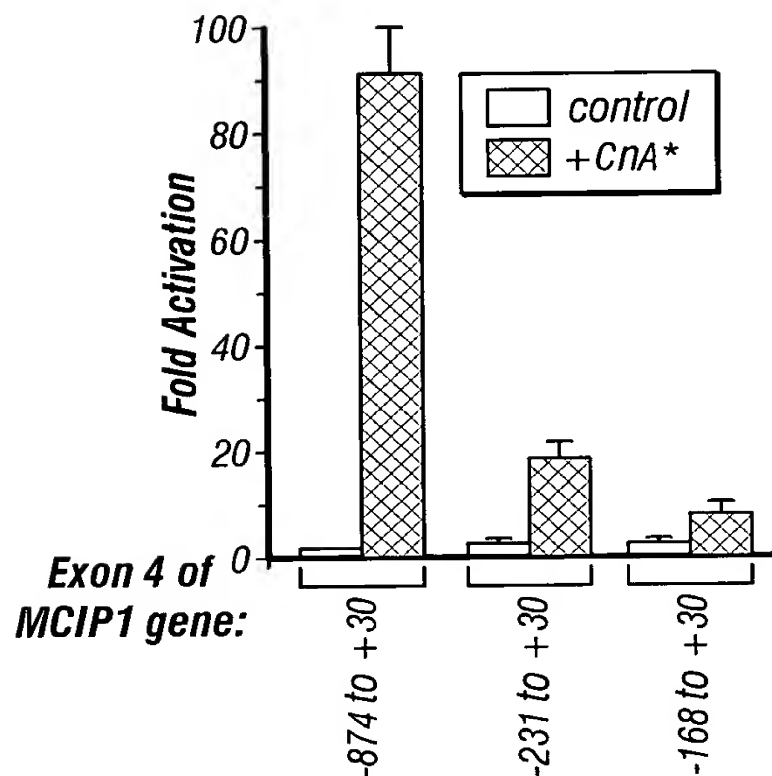


FIG. 8C



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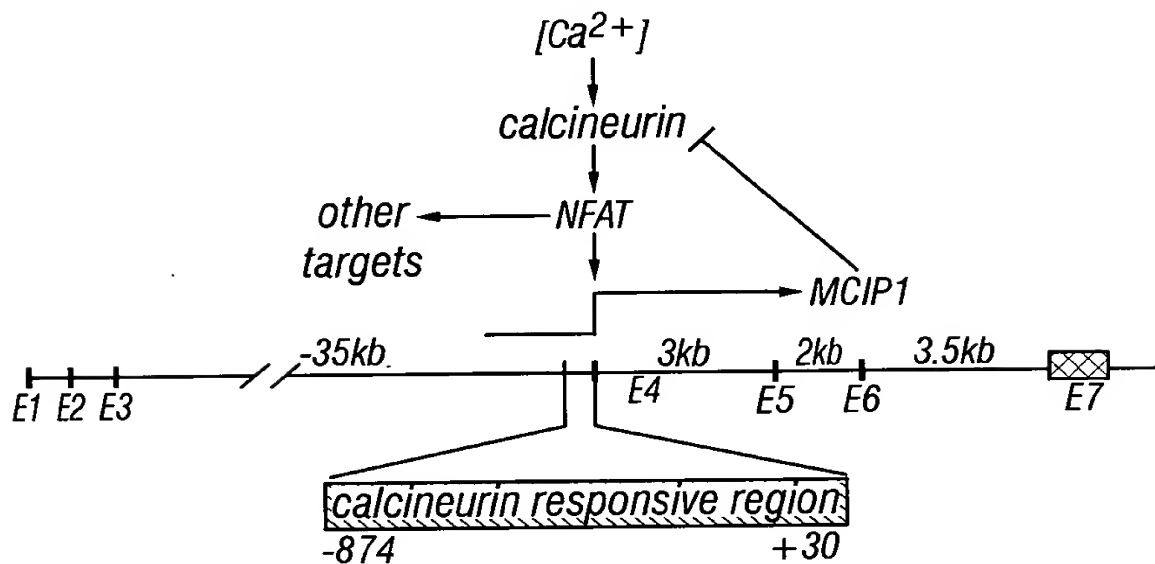


FIG. 9

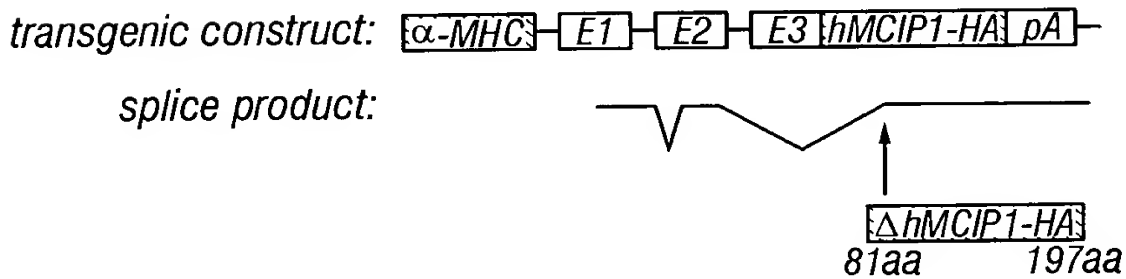


FIG. 10

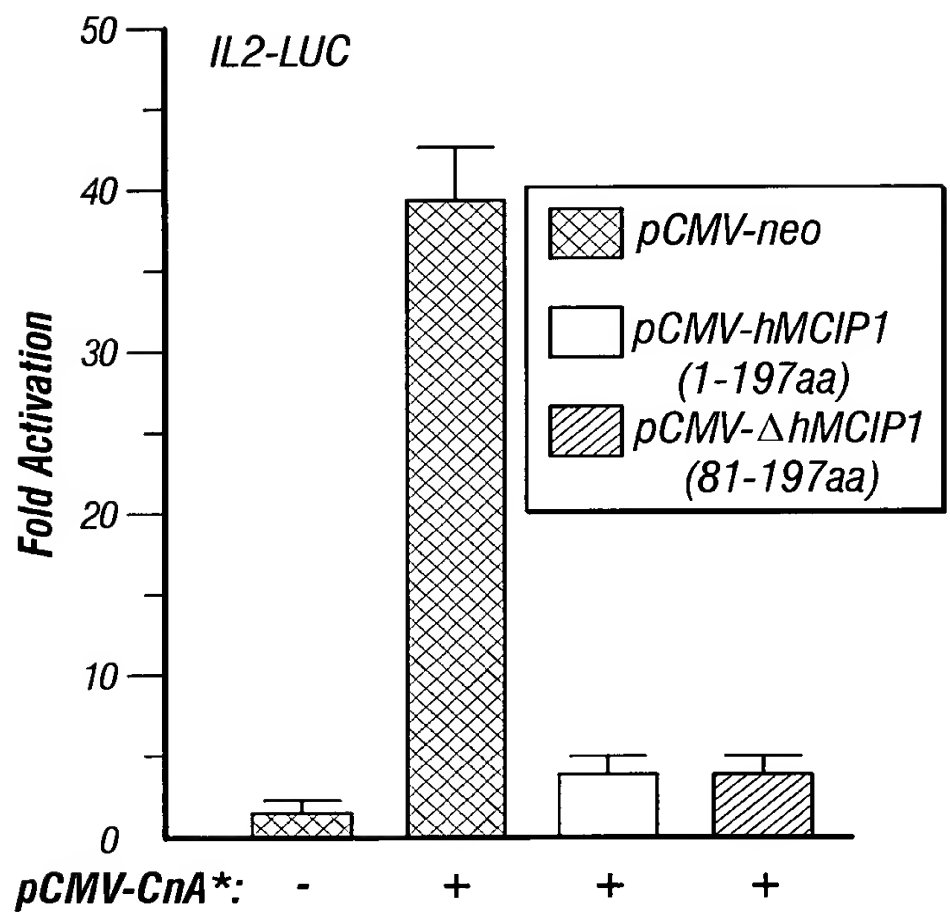


FIG. 11

U.S. Pat. No. 6,811,111 B2
Filed: Jun 16, 2003
Inventor(s): Williams et al.





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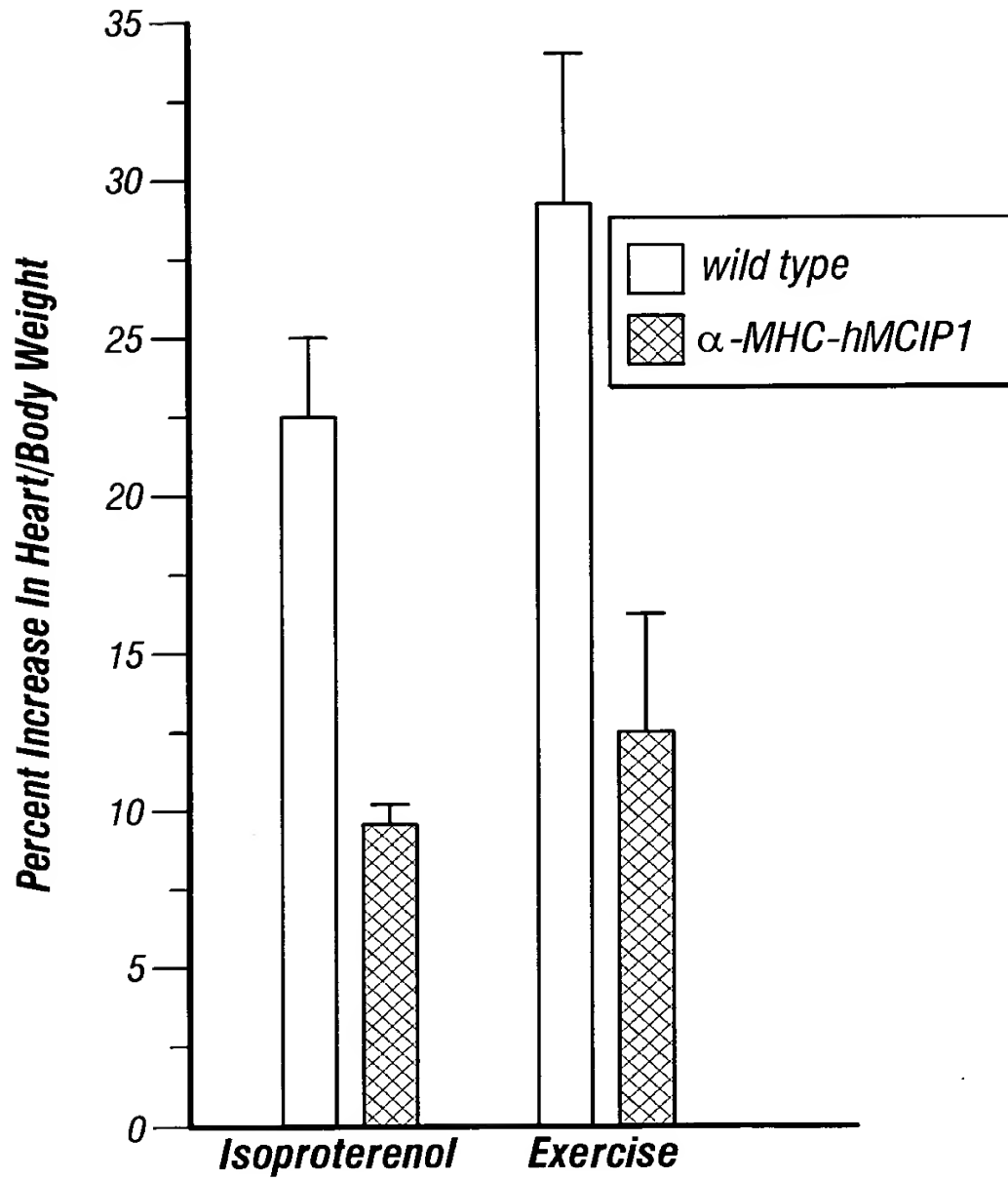


FIG. 12